Prostate Cancer

Prostate Biopsy Schemes and the Detection of Prostate Cancer

Steven R. Potter, MD
Alan W. Partin, MD, PhD
The Brady Urological Institute, The Johns Hopkins Hospital Baltimore

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The widespread use of digital rectal examination (DRE) coupled with measurement of prostate-specific antigen (PSA) for prostate cancer screening has led to a dramatic increase in the number of men undergoing prostate biopsy guided by transrectal ultrasound (TRUS). Systematic parasagittal sextant biopsies have been widely adopted as the standard protocol for prostate biopsy. Significant numbers of men undergo repeat biopsy because of clinical indications (abnormal DRE, elevated PSA) or atypical findings on the initial biopsy. Increases in biopsy number and changes in distribution have recently been proposed in attempts to improve the diagnostic yield of initial biopsy.

Two Consecutive Sets of Transrectal Ultrasound Guided Sextant Biopsies of the Prostate for the Detection of Prostate Cancer

Levine MA, Ittman M, Melamed J, Lepor H.
J Urol. 1998;159(2):471-775.

This prospective nonrandomized study evaluated 137 consecutive men presenting for initial prostate biopsy because of an elevated PSA or abnormal DRE. All men underwent 2 consecutive sets of parasagittal sextant biopsies at a single setting. The initial sextant biopsy revealed cancer in 30 (22%) men, while 13 (10%) men had cancer diagnosed only on the second set of sextant biopsies. Prostate cancer was found on biopsy with decreasing frequency as prostate volume increased, with cancer detected in 43%, 27%, and 24% of men with prostate volumes of <30 cc, 30 to 50 cc, and >50 cc, respectively, on the first set of biopsies.

The authors concluded that the second set of biopsies provided important new information in 20 (28%) men and increased the total number of cancers diagnosed by 30% (Figure). This elegantly designed study provided strong evidence that obtaining more biopsy cores increases diagnostic yield with a minimal increase in potential morbidity. Levine and colleagues also performed a cursory cost analysis that supported obtaining 12 cores at initial biopsy, largely due to the cost savings realized by avoiding a separate set of repeat biopsies in approximately 15% of men. The finding of a lower likelihood of positive biopsy as prostate volume increased was in concordance with previous studies. Levine and colleagues postulated that this was due to the contribution to serum PSA of benign tissue raising overall PSA levels and prompting biopsy of prostates containing small volume cancers that would otherwise not have come to attention. Alternatively, sampling error could be the culprit in large prostates, as any given biopsy would be less likely to find a given volume of cancer in a larger than in a smaller prostate.

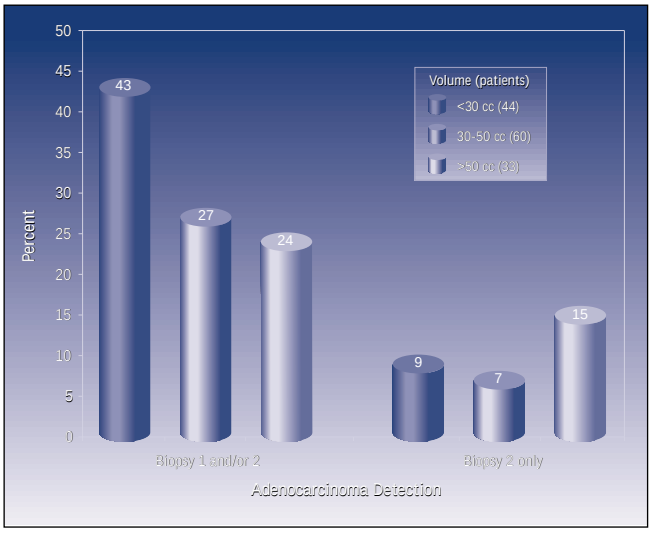

Figure. In men who had large volume prostates, the probability of finding adenocarcinoma only on the second set of sextant biopsies increased approximately 2-fold when compared with men who had smaller volume prostates.

This study argued strongly that more prostate cancers could be found by increasing the number of biopsy cores taken. The relationship of biopsy yield and prostate size remains unsettled. Although increasing biopsy numbers in this study clearly detected more cancers, the relationship between biopsy number and biopsy location as determinants of cancer detection deserves further attention.

Prostate Cancer Detection: Relationship to Prostate Size

Chen ME, Troncoso P, Johnston D, et al.
Urology. 1999;53:764-768.

One of the central difficulties with elucidating the relationship of prostate size and biopsy yield is the fact that prostates without cancer are virtually unavailable for pathologic analysis. Chen and colleagues approached this problem by developing a novel computer simulation that allowed comparison of biopsy results for given prostate and cancer volumes. The authors first evaluated 180 whole-mount radical prostatectomy specimens. The prostates were weighed, step-sectioned, and digitized for computer modeling. Tumor volumes were calculated and compared with prostate volumes. In all, 607 tumors in 180 prostates were quantified. Computer simulated biopsy runs were then performed on the digitized prostates. Sextant biopsies in glands weighing ≤50 g and glands >50 g were positive in 67% and 48% of cases respectively. Small volume cancers were more prevalent in larger prostates.

The authors concluded that biopsy rates in large glands were lower than in small glands because biopsy of larger glands is often driven by elevations of PSA that may be produced by benign prostate tissue. They argued that if sampling error were the primary reason for the consistent finding of lower biopsy yields in larger prostates, larger volume cancers would preferentially be found in large prostates. Chen and associates recommended against obtaining extra biopsies solely because of larger prostate size, arguing that this would likely detect a disproportionate number of small-volume cancers. The question of optimal biopsy sites and biopsy number (independent of prostate volume) is still unanswered.

Comparison of Prostate Biopsy Schemes by Computer Simulation

Chen ME, Troncoso P, Tang K, et al.
Urology. 1999;53:951-960.

The logical application for the biopsy simulation model developed by Chen and colleagues was in the evaluation of optimal biopsy schemes. Digitized data from 180 whole-mount prostates used for evaluation of prostate size and biopsy results were used again. Forty simulations were performed on each prostate using 10 separate biopsy schemes. These ranged from a 2 core near apical scheme to an 18 core, 5-region peripheral zone protocol. Altogether, over 1 million individual biopsies were simulated and evaluated.

For biopsy protocols limited to the transition zone, increasing the number of biopsy cores taken increased the detection rate of cancer. However, the number of cores taken was clearly not the sole determinant of detection rate. For example, an 8-core protocol including parasagittal sextant and 2 transition zone biopsies detected more cancers than an 8-core protocol that biopsied only the peripheral zone. The biopsy scheme that performed best overall was an 11-core multisite directed biopsy set that included routine sextant, 1 posterior midline, 2 transition zone, and 2 anterior horn cores. This 11-core model detected 85% and 70% of the cancers in prostates ≤50 g and >50 g respectively, outperforming the 13-core and 18-core protocols.

Chen and associates concluded that cancer detection rates were not determined solely by the number of biopsies taken. They have shown that the routinely performed parasagittal sextant biopsy would detect significantly fewer cancers than protocols including transition zone biopsies.

Prospective Randomized Trial Comparing 6 Versus 12 Cores: Effect on Cancer Detection Rate

Miller DC, Naughton CK, Mager DE, et al.
J Urol. 1999;161(4 suppl):291. Abstract 1130.

Miller and colleagues initiated a prospective trial to compare 12-core and 6-core biopsy protocols. They randomized 240 men, all with serum PSA <20 ng/mL, to a standard parasagittal sextant scheme or a 12-core scheme that included sextant biopsies and 6 additional lateral cores. At least 1 set of prior negative biopsies had been performed in 101 (42%) of these men. The men receiving 6- and 12-core biopsies had similar ages, PSA levels, prostate volumes, and likelihood of prior negative biopsy.

Prostate cancer was found in 27% and 26% of all men after 6-core and 12-core biopsy, respectively. Cancer detection was, therefore, not improved by the addition of 6 additional biopsy cores. The authors evaluated these biopsy schemes by subgroups, including history of prior biopsy, prostate volume, race, and PSA level, finding no increase in cancer detection with the 12-core biopsy technique for any subgroup.

Because many of these men had negative biopsies before entry into the study, the rate of positive biopsies was lowered in both groups. This could potentially mask differences between the standard and 12-core groups. Controversy continues to surround the optimal number and placement of biopsies for the detection of prostate cancer. Clearly, simply increasing the number of cores taken may not be an ideal solution. Numerous investigators have found that cancer detection is improved most when far lateral peripheral zone biopsies are added to routine parasagittal protocols. A prospective, randomized comparison of biopsy techniques in a population of men without prior biopsy would add significantly to understanding of these issues. □